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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/808,314	03/14/2001	Randall W. Nelson	41821.0236	3078

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EXAMINER

COUNTS, GARY W

ART UNIT	PAPER NUMBER
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1641

DATE MAILED: 06/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/808,314

Applicant(s)

NELSON ET AL.

Examiner

Gary W. Counts

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 May 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14, 20-29, 31-33, 35-40, 42, 44-46 and 48 is/are pending in the application.
4a) Of the above claim(s) 1-14 and 20-29 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 31-33, 35-40, 42, 44-46 and 48 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the claims

The amendment and declaration filed May 10, 2004 is acknowledged and has been entered.

Rejections Withdrawn

The Declaration by Allan L. Bieber filed May 10, 2004 is found persuasive. Therefore, the 102 and 103 rejections using the article "Mass Spectrometric Immunoassay" published in Analytical Chemistry 1995, 67, 1153-1158 has been withdrawn. However, new ground(s) of rejection is made (see below).

Oath/Declaration

1. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: The address of Inventor Krone is crossed out but not initialed and no date of amendment has been disclosed.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 37-40, 42, 44-46 and 48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 33, part (b) "the constant amount" there is no antecedent basis for this limitation. It is recommended to change "constant amount" to --known amount--.

Claim 37, the recitation "plurality of distinct internal reference species" is vague and indefinite. It is unclear if applicant is referring to many different kinds of internal reference species or many of the same kind of internal reference species which is distinct from the analyte. Please clarify.

Claim 39, part (b) "the constant amount" there is no antecedent basis for this limitation. It is recommended to change "constant amount" to --known amount--.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 31 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Gaskell et al (Immunoabsorption to Improve Gas Chromatography/High-Resolution Mass Spectrometry of Estradiol-17B in Plasma, Clin. Chem. 29/4, 677-680 (1983)).

Gaskell et al disclose a method for detecting at least one analyte in which an internal standard is added to the sample containing the analyte. Gaskell et al disclose capturing and isolating the analyte and internal standard with an affinity reagent (solid phase antiserum). Gaskell et al disclose that this extract containing the analyte and internal standard is analyzed by GC-MS. Gaskell et al disclose that a standard curve is used for the quantitation of the analyte and internal standard (p 678). Gaskell et al

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disclose that the standard curve was established by analysis of derivatized standard mixtures.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 31-33 and 37-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Papac et al (Epitope mapping of the gastrin-releasing peptide/anti-bombesin monoclonal antibody complex by proteolysis followed by matrix-assisted laser desorption ionization mass spectrometry, Protein Science (1994), 3:1485-1492) in view of Gaskell et al (Immunoabsorption to Improve Gas Chromatography/High-Resolution Mass Spectrometry of Estradiol-17B in Plasma).

Papac et al disclose antibodies immobilized to agarose beads (solid substrate). Papac et al disclose incubating these beads with antigens for a time period to allow the immobilized antibody to bind to the antigen to form a complex (post-combination affinity reagent) (p. 1486, col 2, Results Section). Papac et al disclose centrifuging the complex and removing supernatant (isolating the post-combination affinity reagent). Papac et al disclose adding matrix (laser desorption/ionization agent) to the antibody/antigen complex (p. 1486, col 2). Papac et al disclose determining the identity of the analyte using mass spectrometry (p. 1486, col 2 and Figure 1). Papac et al disclose determining the analyte by m/z (mass to charge ratio) (Figure 1).

Papac et al differ from the instant invention in failing to teach the specimen is combined with an internal reference species of known concentration prior to the capturing and isolation step wherein both the analyte and the IRS are captured and isolated.

Gaskell et al disclose the addition of an internal standard to a specimen containing analytes and determining the analyte by mass spectrometry. Gaskell et al disclose capturing and isolating the analyte and internal standard with an affinity

reagent (solid phase antiserum). Gaskell et al disclose that a standard curve is used for the quantitation of the analyte and internal standard (p 678). Gaskell et al disclose that the standard curve was established by analysis of derivatized standard mixtures.

Gaskell et al disclose that the addition of the internal standard to the specimen provides higher precision to the analytical procedures (p. 677 & 679). Gaskell further discloses that the immunoadsorption technique provides a rapid and convenient procedure for an analyte before analysis (p. 679).

It would have been obvious to one of ordinary skill in the art to incorporate an internal standard and affinity reagents as taught by Gaskell et al into the method of Papac et al because Gaskell et al teaches that the addition of the internal standard to the specimen provides higher precision to the analytical procedures and also teaches that the immunoadsorption technique provides a rapid and convenient procedure for an analyte before analysis (p. 679).

10. Claims 35, 36, 40 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Papac et al (Protein Science) and Gaskell et al in view of Papac et al (Direct analysis of Affinity-Bound analytes by MALDI/TOF MS, Analytical Chemistry 194, 66, 2609-2613).

See above for teachings of Papac et al (Protein Science).

Papac et al (Protein Science) differ from the instant invention in failing to disclose adding a disassociation agent to the isolated post-combination affinity reagent prior to the step of adding the laser desorption/ionization agent.

Papac et al (Direct analysis of Affinity-Bound analytes by MALDI/TOF MS) disclose sample preparation can influence the spectra observed and that for immobilized affinity chromatography, a 3 times stronger signal is observed when the supernatant is used for analysis (a dissociation reagent is used before application of the desorption/ionization agent) compared with mixing the MALDI matrix with the beads on the target (p. 2613, 3rd paragraph) and that immobilized affinity chromatography differs from conventional chromatography in that it exploits specific biological interactions such as those of an antibody and antigen which demonstrate high specificity associated affinity binding and that, either half of a biological interaction can be used in the stationary phase as an immobilized ligand (p. 2609, paragraph 1).

It would have been obvious to one of ordinary skill in the art to incorporate the use of a dissociation reagent as taught by Papac et al (Direct analysis of Affinity-Bound analytes by MALDI/TOF MS) into the modified method of Papac et al (Protein Science) because Papac et al (Direct analysis of Affinity-Bound analytes by MALDI/TOF MS) show that this dissociation reagent allows for a 3 times stronger signal.

11. Claims 44-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Papac et al (Protein Science) and Gaskell et al in view of Merren (US 3,770,337).

See above for teachings of Papac et al and Gaskell et al.

Papac et al (Protein Science) and Gaskell et al. differ from the instant invention in failing to specifically teach interpolating the analyte species mass spectrometric response to the IRS's mass spectrometric response.

Merren teaches the addition of reference substance which provides a spectrum containing peaks at several known mass-to-charge ratios. Merren teaches that the reference spectrum is accurately correlated with the spectrum of the unknown substance, therefore the reference peaks act as accurate markers forming a calibrated scale from which the mass-to-charge ratios of peaks of the unknown substance is interpolated. Merren teaches that this provides a method for combining signals representative of the simultaneous spectral analysis of two substances, thereby permitting single channel processing of the combined signal (col 1, lines 53 – col 2, lines 19).

It would have been obvious to one of ordinary skill in the art to interpolating the analyte species and the reference species as taught by Merren into the modified method of Papac et al (Protein Science) because Merren shows that this provides a method for combining signals representative of the simultaneous spectral analysis of two substances, thereby permitting single channel processing of the combined signal.

12. Claim 48 is rejected under 35 U.S.C. 103(a) as being unpatentable over Papac et al (Protein Science) and Gaskell et al in view of Papac et al (Direct analysis of Affinity-Bound analytes by MALDI/TOF MS, Analytical Chemistry 194, 66, 2609-2613) as applied to claims 31-33, 35-40 and 42 above, and further in view of Merren (US 3,770,337).

See above for teachings of Papac et al (Protein Science), Gaskell et al and Papac et al (Direct Analysis of Affinity-Bound).

Papac et al (Protein Science), Gaskell et al. and Papac et al (Direct Analysis of Affinity-Bound) differ from the instant invention in failing to specifically teach interpolating the analyte species mass spectrometric response to the IRS's mass spectrometric response.

Merren teaches the addition of reference substance which provides a spectrum containing peaks at several known mass-to-charge ratios. Merren teaches that the reference spectrum is accurately correlated with the spectrum of the unknown substance, therefore the reference peaks act as accurate markers forming a calibrated scale from which the mass-to-charge ratios of peaks of the unknown substance is interpolated. Merren teaches that this provides a method for combining signals representative of the simultaneous spectral analysis of two substances, thereby permitting single channel processing of the combined signal (col 1, lines 53 – col 2, lines 19).

It would have been obvious to one of ordinary skill in the art to interpolating the analyte species and the reference species as taught by Merren into the modified method of Papac et al (Protein Science) because Merren shows that this provides a method for combining signals representative of the simultaneous spectral analysis of two substances, thereby permitting single channel processing of the combined signal.

Double Patenting

Claims 31 and 37 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 31-50 of

compending Application No. 09/024,988. Although the conflicting claims are not identical, they are not patentably distinct from each other because although the claims of application 09/808,314 do not require that the IRS is a modified analyte with shifted molecular weight as independent claim 31 in application 09/024,988 one of ordinary skill would recognize that the claims of 09/024,988 would encompass the claims of 09/808,314

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicant's arguments filed May 10, 2004 have been fully considered but they are not persuasive.

102 rejections

Applicant argues that Gaskell is specifically directed to establishing fractionation procedures that complement the specificity of gas chromatography-mass spectrometry (GC-MS) detection and that Applicant's claimed methods do not require gas chromatography either before, or in combination with, mass spectrometry in order to achieve detection. This is not found persuasive because the instantly recited claims only require using mass spectrometric analysis to determine the amount of analyte. It is noted that the claims have open language and therefore can contain other components and the argument that Gaskell teaches gas chromatography in their method is therefore

moot. Unless there is a recitation in the claims, which excludes other components, the claims as recited encompass the teachings of Gaskell et al.

Conclusion

13. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.


Kolhouse et al disclose adding multiple internal standards to a specimen which is analyzed by mass spectrometry (col 8, lines 38-68).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary W. Counts


LONG V. LE
SUPERVISORY PATENT EXAMINER
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